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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/090,183	03/02/2002	Ralph A. Reisfeld	TSRI 829.0	4743

7590 02/24/2005

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EXAMINER	
BURKHART, MICHAEL D	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 02/24/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/090,183	REISFELD ET AL.	
	Examiner	Art Unit	
	Michael D. Burkhart	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 November 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1,2,4-8,10 and 32-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-8,10 and 32-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 3 and 9 were canceled in the response dated 11/23/04. Claims 1, 2, 4-8, 10, and 32-34 are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 2, 4-8, 10, and 32-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

This rejection is maintained for reasons of record in the previous Office Action and for reasons outlined below. Applicants traverse this rejection by asserting that ample experimental data were presented in the application and that the murine model is acceptable because murine Flk-1 shares an 85% homology with human KDR. Applicants also claim the references cited in the enablement rejection of the prior Office Action are "inapposite" and "inadmissable hearsay". In this regard, applicants' are confusing patent prosecution with rules governing evidence in court proceedings.

Applicant's arguments filed 11/23/2004 have been fully considered but they are not persuasive. First, the rejection is for lack of enablement, not for lack of novelty (i.e. a prior art rejection), and as such there is no requirement that the references qualify as prior art. Second,

because the references are publications from peer-reviewed scientific journals, they represent the polar opposite of "hearsay".

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation (*United States v. Telectronics,* Inc. 8 USPQD2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is required is a conclusion reached by weighing several factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQQ2d 1400 (Fed. Cir. 1988) and include the following:

Unpredictability of the art. As stated previously, the art concerning DNA vaccines (particularly in humans) and the use of mouse models to assay efficacy in humans is unpredictable. Applicants argue that Garmory et al. militates against the enablement rejection because it states "..*Salmonella* vaccines look very promising.", some *S. Typhi* strains "..have been shown to be immunogenic in clinical trials.", and that immunity has been achieved in animal models. Stating that a vaccine looks promising does not equal teaching how to make and use, i.e. the requirements for enablement. Demonstrating immunogenecity does not equal vaccination, i.e., a protective level of immunity, and, finally, the problems with animal models of human disease were discussed in the previous Office Action, and below.

Applicants argue that Restifo et al is not a prior art reference, as it does not suggest the instantly claimed vaccine. This was never the intention, as Restifo et al was not used as a prior art reference. Applicants state the Gura reference does not apply because it reviews problems with murine models of anticancer drugs and that the present claims are not directed to anticancer drugs, but instead to DNA vaccines. Applicants are reminded of the title of the invention "DNA

vaccines against proliferating endothelial cells...", and the language of claim 1, "..against proliferating endothelial cells..". As such, the claims are indeed directed to cancer therapy, i.e. the treatment of unchecked or unnatural proliferation of cells.

Applicants argue that Steinman et al is an "..undated historical account.." and sheds no light on the enablement issues in the instant application. Because applicants seek to extend anti-tumor DNA vaccine results in mice to the same in humans, Steinman et al is particularly relevant. They state "..spontaneous human malignancies differ fundamentally from experimental mouse tumors, and the human and mouse immune systems differ considerably from one another." Given this, applicants disclosure has two crucial enablement problems: the mouse tumors of the disclosure are not representative of human tumors; and the immune response of the mice to the instant DNA vaccine is not predictive of the human immune response.

State of the art. The state of the art regarding the treatment of cancer by vaccination, while represented voluminously in the literature, is poorly developed. No DNA vaccine to date has been shown to be efficacious in this regard.

Number of working examples. Applicants have provided a working example of a DNA vaccine to treat tumors in mice. Applicants have provided no working examples of a DNA vaccine that can induce an effective human immune response to proliferating endothelial cells.

Amount of guidance. Applicants provide no direction for the claimed vaccine regarding use and efficacy in humans. The specification requires the skilled artisan to practice trial and error experimentation with human VEGF receptor sequences, delivery vectors, and adjuvants to determine which (if any) will be efficacious as claimed.

Scope of the invention. The claims are broad in nature and read on any VEGF receptor-based DNA vaccine.

Nature of the invention. The invention involves the unpredictable art of producing an effective immune response to proliferating endothelial cells in humans.

Level of skill in the art. While the level of skill in the art is high, the unpredictability of the art, lack of guidance, broad scope of the claims and poorly developed state of the art would require that undue and excessive experimentation would have to be conducted by the skilled artisan in order to practice the claimed invention.

Given the above analysis of the factors which the courts have determined are critical in determining whether a claimed invention is enabled, it must be considered that undue and excessive experimentation would have to be conducted by the skilled artisan in order to practice the claimed invention.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael D. Burkhart whose telephone number is (571) 272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael D. Burkhart
Examiner
Art Unit 1636

DAVID GUZO
PRIMARY EXAMINER